11:00

883-3 Dobutamine-Induced Changes in Regional Myocardial Function Are Caused by a Mismatch Between Cardiac Work and Coronary Flow in the Presence of a Significant Coronary Artery Stenosis

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Background: Dobutamine (Dob) is a widely used agent for producing ischemic wall motion (WM) abnormalities during dobutamine-stress echocardiography (Echo). However, the exact pathophysiologic mechanism of this phenomenon has not been adequately studied.

Methods: Dob-stress-induced regional myocardial function (RMF) was assessed in relation to changes in cardiac work and coronary flow (CF) distal to 20 stenotic coronary arteries (StCA) (80 ± 14%) with a 0.014 Doppler flowire. Incremental iv Dob (5–40 μg/kg/min) was administered. Average peak CF velocity (APV, cm/sec), heart rate-pressure product (RPP) coronary perfusion pressure (CPP) (Mean Ao P-LVEDP) and WM score (1 = normal to 4 = dyskinetic) were calculated.

Results:

	C	Dob10	Dob20	Dob30	Peak Dob
CPP	88 ± 13	94 ± 11	95 ± 14	93 ± 12	94 ± 16
RPP	10604 ± 1755	11008 ± 2144	13264 ± 3088*	15675 ± 4085*°	17515 ± 4085*°
%Δ	-	4 ± 14	25 ± 20	48 ± 22	67 ± 42
APV	10.5 ± 5.1	11 ± 5.2	15.7 ± 7.6*	17.6 ± 7.6	17.3 ± 7.4
%Δ	-	6 ± 18	61 ± 58	87 ± 74	91 ± 93
RMF	1.83 ± 0.81	1.61 ± 0.64	1.61 ± 0.64	-	2.1 ± 0.7*

*p < 0.05 vs C, °p < 0.05 vs Dob20, p < 0.05 vs Dob20 or Dob30 respectively.

Conclusion: At low dose Dob stress there is no significant change in CF while there is a slight improvement in WM. At intermediate Dob dose the WM improvement is sustained as cardiac work and CF both increase significantly. At peak Dob stress, WM deterioration results from a mismatch between the significant further increase in cardiac work and an insignificant further increase in CF, which proves inadequate to compensate for the increased oxygen requirements.

11:15

883-4 Preservation of Coronary Blood Flow in Humans by Esmolol During Dobutamine

M. Dolan, M. Kern, R. Bach, R. Castello, T. Donohue, C. Mechem, J. St. Vrain, F. Dressler, A. Labovitz. *St Louis University School of Medicine, USA*

The efficacy of beta-blockers during acute myocardial infarction is well established. However, their effect during acutely induced ischemia on left ventricular function and coronary blood flow is not described. Therefore, we studied the effects of intravenous beta-blocker (Esmolol) during Dobutamine (Dob) induced acute ischemia in 21 patients using Stress Echocardiography (DSE) before and again after Esmolol (titrated to 24 mg/min). Post-stenotic coronary blood flow velocity (CBFV), heart rate (HR), blood pressure (BP), at base and peak Dob infusion with and without Esmolo (E) were compared.

	Peak CBFV	%Δ CBFV	HRxBP	HR
Dobutamine (D)				
Positive (Pos)	19 ± 16	33 ± 67	17582 ± 3903	117 ± 18
Negative (Neg)	26 ± 17	72 ± 50	14444 ± 3207	118 ± 19
P	NS	NS	NS	NS
Dobutamine & Esmolol (D-E)				
Positive	19 ± 10	30 ± 47	13983 ± 3554	83 ± 12
Negative	18 ± 10	36 ± 42	11211 ± 2184	76 ± 15
P	NS	NS	0.05	NS
P*	NS	NS	0.0003	0.001
P**	0.01	0.01	0.01	0.001

P = pos vs neg, P* = posD vs posD-E, P** = negD vs negD-E

After Esmolol, during positive DSE, myocardial demand (BPxHR) is reduced, CBFV is maintained; while during negative DSE, CBFV decreased (26 ± 17 vs 18 ± 10, p < 0.01) with decrease in myocardial oxygen demand.

Conclusion: Under ischemic stimulation, Esmolol favorably altered coronary auto-regulation preserving CBFV for any increase in myocardial oxygen demand.

11:30

883-5 Alternation in Collateral Flow Dynamics as a Determinant of Stress-Induced Myocardial Ischemia in Humans

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Background: It is still unclear whether myocardial ischemia is associated with the change in collateral flow dynamics during myocardial stress in patients with coronary artery disease and coronary collaterals.

Methods: Myocardial contrast echocardiography was performed by injecting sonicated contrast medium into the right coronary artery (RCA) before and immediately after rapid atrial pacing in 20 patients with angiographically evidenced coronary collaterals to the occluded left anterior descending coronary artery from the RCA. The peak background-subtracted contrast intensity (PCI) in the collateral territory and its ratio to that in the control territory were compared between patients with (n = 9) and without (n = 11) lactate production (LP) in the collateral territory during rapid atrial pacing.

Results: 1) PCI and PCI ratio before pacing did not differ between patients with and without LP (PCI: 13.8 ± 19.1 U vs 16.2 ± 13.3U, p = 0.75; PCI ratio: 0.70 ± 0.71 vs 0.87 ± 0.65, p = 0.58, respectively). 2) However, both PCI and PCI ratio were decreased by atrial pacing more significantly in patients with LP than in those without (PCI: −67 ± 53% vs −15 ± 34%, p < 0.05; PCI ratio: −68 ± 45% vs −8.2 ± 32%, p < 0.05, respectively). 3) Regional wall motion at baseline, severity of the donor RCA stenosis, and other baseline characteristics were similar between patients with and without LP.

Conclusion: These data suggested that provocation of myocardial ischemia was closely associated with alternation in collateral flow dynamics during stress, rather than the extent of collateral flow at rest in patients with angiographically evidenced coronary collaterals.

11:45

883-6 Coronary Vasospasm as a Source of False Positive Results During Dobutamine Echocardiography

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Background: Dobutamine can induce coronary vasoconstriction through alpha-1 adrenoreceptor stimulation, and anecdoctical cases of dobutamine induced coronary vasospasm have been reported. The aim of the study was to assess whether coronary vasospasm can be a significant source of false positive results during dobutamine stress.

Methods: We considered 254 consecutive patients who underwent dobutamine echocardiography (up to 40 μg/kg/min and atropine 1 mg if needed) before coronary angiography, and we analyzed the 54 patients (35 men, 19 women, mean age 49 ± 10 years) with a normal angiogram.

Results: During the angiography spontaneous coronary artery spasm occurred in 6 patients. Dobutamine stress echo was positive in 6 out of 6 patients with, and only in 7 out of the 48 patients without angiographically assessed coronary vasospasm (100% vs 14%, p < 0.01). Out of the 6 patients with positive dobutamine stress echo 5 reported chest pain during the examination, but only 2 had additional ECG changes. In all patients with angiographically documented vasospasm the regions showing dobutamine induced dysfunction were supplied by the coronary with angiographically documented spasm.

Conclusion: Coronary artery spasm can be an important source of false positive results during dobutamine stress echocardiography.

884 Atrial Fibrillation: Conversion and Suppression

Wednesday, April 1, 1998, 10:30 a.m.–Noon
Georgia World Congress Center, Room 267W

10:30

884-1 Oral Dofetilide for Conversion of Patients With Chronic Atrial Fibrillation or Atrial Flutter to Normal Sinus Rhythm: A Multicenter Study

S.N. Singh, M.R. Berk, L.G. Yellen, R.G. Zoble, D. Abrahamson, C. Satler, T. Friedrich. *Veterans Affairs Medical Center, Washington, DC, USA*

Dofetilide, a class III anti-arrhythmic agent is a potent selective potassium channel blocker being developed for a broad range of tachyarrhythmias including atrial fibrillation and atrial flutter (AF/AF1). We examined the efficacy and safety of oral dofetilide for converting patients with chronic AF/AF1 to normal sinus rhythm (NSR) in a double-blind, placebo-controlled multicenter

study. Three hundred twenty-five patients[277AF/48AF1; 84% male; average age = 67 years; duration of AF/AF1 = 2 weeks–7 months; NYHA: I = 28%, II = 64%, III = 8%] were randomized to 1 of 4 treatment groups:

Dofetilide 125 mcg, 250 mcg, 500 mcg, or placebo BID. The number of patients who achieved NSR after 3 days of oral dosing were as follows: placebo 1/82 (1%), dofetilide 125 mcg 5/74 (6%), dofetilide 250 mcg 8/79 (10.1%), dofetilide 500 mcg 23/71 (32%). Adverse effects were balanced across treatment groups. No torsades nor deaths occurred.

Conclusion: We conclude that orally administered dofetilide at 500 mcg BID is effective and safe in converting chronic atrial fibrillation/flutter to normal sinus rhythm.

10:45

884-2 Intravenous Propafenone Versus Digoxin in Recent Onset Atrial Fibrillation. A Placebo-controlled, Randomized Study

L. Bianconi. *On behalf of PAFIT-3 Investigators; S. Filippo Neri Hospital, Rome, Italy*

Background: Intravenous propafenone (Prop) has been shown to effectively restore sinus rhythm in recent onset atrial fibrillation (AF), while the efficacy of iv digoxin (Dig) has been questioned. However, a direct comparison among these drugs and placebo (Plac) is still lacking.

Methods: One hundred twenty three pts with AF lasting <72 hrs were randomized to either iv Prop (2 mg/Kg, 41 pts) or iv Dig (0.5 mg, 40 pts) or Plac (42 pts). After 1 hour, non-converted Prop or Dig pts were switched to the other drug, while non-converted Plac pts were randomized to either iv Prop or Dig and monitored for a further hour.

Results: After the first treatment, 20/41 (49%) Prop pts were cardioverted, versus 13/40 Dig pts (32%) and 6/42 Plac pts (14%). The table reports the relative efficacy (RE) of the drugs calculated by logistic regression analysis. Among the 47 pts resistant to the first treatment who were switched to the alternative drug, Dig was effective in 1/20 pts (5%) and Prop in 13/27 (48%) pts ($p < 0.05$). In the 35 non-converted Plac pts allocated to an active drug, sinus rhythm was obtained in 10/19 pts (53%) by Prop and in 1/16 pts (5%) by Dig ($p < 0.05$). Considering all the 116 pts who received a drug as a first active treatment, conversion rates were 50% (30/60 pts) with Prop and 25% (14/56 pts) with Dig ($p < 0.01$, C.I. 95%1.2–3.4). No significant side effects were observed in any pts.

	RE	C.I. 95%	p
Prop vs Plac	3.41	1.53–7.63	<0.01
Dig vs Plac	2.27	0.96–5.40	NS
Prop vs Dig	1.50	0.97–2.59	NS

Conclusion: In recent onset AF iv propafenone restores sinus rhythm more effectively than either placebo or iv digoxin.

11:00

884-3 Efficacy and Safety of Intravenous Flecainide Compared to Oral Quinidine for Conversion of Acute Atrial Fibrillation (AF) to Sinus Rhythm in Patients Pretreated With Intravenous Metoprolol – The FLEQUIN Trial

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Objectives: We studied the efficacy and safety of i.v. flecainide compared with oral quinidine for the conversion of acute AF after i.v. metoprolol was given to lower ventricular rate.

Background: Effective and safe treatment of acute AF is needed in the emergency room. A delay in conversion to sinus rhythm (SR) prolongs the hospital treatment and increases costs.

Methods: A randomised, double blind comparison between flecainide (2 mg/kg within 30 min.) and quinidine (200 mg up to 3 times 2 hr apart) was performed in 163 patients with acute (<48 hours) AF after metoprolol was given openly.

Results: SR was restored within three hours in 45 (54%) of the 83 patients in the flecainide group and in 24 (30%) of the 80 patients in the quinidine group ($p = 0.0018$). DC cardioversion was needed in 23% and 19% of patients (N.S.), and the median delays to SR were 0.6 hours and 4.1 hours in the flecainide and quinidine groups, respectively ($P < 0.001$). The median hospital stay of patients not needing DC cardioversion and prolonged hospital stay (>48 hr) was 6.4 hr in the flecainide group and 9.4 hr in the quinidine group, ($p = 0.012$). Asymptomatic pauses of 3–9.8 seconds were found in ambulatory ECG recording of 8 patients in the flecainide group and of 7 patients in the quinidine group. Two patients in the flecainide group had a short lasting circulatory collapse.

Conclusions: Flecainide acted more rapidly in restoring SR than quinidine. Both drugs were safe for the treatment of outpatients in the emergency room. I.v. metoprolol was a safe pretreatment for patients treated with either flecainide or quinidine.

11:15

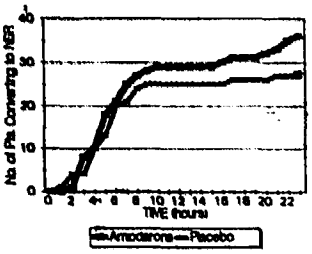
884-4 Acute Atrial Fibrillation: High-Dose IV Amiodarone Facilitates Conversion to Normal Sinus Rhythm. When Is It Necessary?

G. Cotter, E. Cotter-Metzkor, E. Kaluski, A. Blat, Y. Moshkovitz, I. Litinsky, M. Koren, R. Zaldenstein, A. Golik. *Assaf-Harofeh Medical Center, Zerifin, Israel*

The rate of spontaneous conversion of acute atrial fibrillation (Ac AF) to normal sinus rhythm (NSR) is high and not affected by low dose amiodarone (Am.) treatment. We evaluated high-dose Am. in the treatment of Ac AF.

Methods: Eighty patients (pts.) with paroxysmal AF, admitted for Ac. AF (<48 h) were randomized to receive for 24 hours: (1) Group A, (n = 40): Placebo (2) Group B, (n = 40): Continuous IV Am. 120 mg/hour (total 3 g). Group A pts. not converting to NSR within 24 hr were crossed over to Am therapy. All pts. received Digoxin.

Results: Baseline pulse was 127 ± 19 beats/min. and ± 21 beats/min. in groups A and B. In group A, 27 pts. (67%) converted to NSR vs. 36 (90%) in group B ($p = 0.029$). Twenty-five of 27 (93%) pts. converting spontaneously (in group A) have converted within 12 hours. Eleven pts. (85%) in group B not converting on placebo have converted after being crossed over to high-dose Am. treatment. Finally, 6 pts. (in both groups) did not convert on high-dose Am., 3 converted after electrical cardioversion, but all 6 were in chronic AF after 1 month. In pts. still in AF after 8 hours of treatment, the pulse rate decreased to 114 ± 20 beats/min. in group A vs. 83 ± 15 beats/min. in group B ($p = 0.0014$). No adverse events requiring treatment occurred in group B pts.



Conclusion: IV high-dose Am. treatment (120 mg/hr) is safe and facilitates conversion of Ac AF to NSR. Spontaneous conversion commonly occurs within 12 hours, therefore, high-dose Am. may be reserved for pts. requiring rate control, long term Am. treatment or not converting within 12 hours. Pts resistant to high-dose Am. are at high risk of developing chronic AF.

11:30

884-5 Class III Drugs for Suppression of Recurrent Symptomatic Atrial Fibrillation

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Background: In this comparative trial, we examined the efficacy and safety of amiodarone and sotalol in maintaining normal sinus rhythm in patients (pts) with refractory atrial fibrillation.

Methods: Seventy consecutive pts (39 men, mean age 63.1 ± 9 years) were randomized into two clinically similar groups: 35 received amiodarone and 35 sotalol. Pts with ejection fraction ≤40% or clinically significant heart disease were excluded. The amiodarone dosage began with 800 to 1600 mg/day for 7 to 14 days orally and was then tapered over 7 to 12 days, generally to 200 mg/day. The sotalol dosage was 160–360 mg/day, as tolerated. Follow up clinical evaluations were conducted at 2 month intervals for the first 6 months and at 3 month intervals thereafter. The proportion of pts remaining in sinus rhythm was calculated for the two groups using the Kaplan-Meier method.

Results: Ten of the 35 pts on amiodarone developed atrial fibrillation during the 12-month observation period, compared to 21 of the sotalol group ($p = 0.008$). Progression to atrial fibrillation was faster in the sotalol pts ($p = 0.012$): after 6 months, 77.4% of amiodarone pts remained in normal sinus rhythm compared to 54.3% of the sotalol pts, while at 12 months the respective percentages were 71% and 40%. Sex, age, left atrial size and atrial fibrillation type had no significant effect.